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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,240	03/23/2005	Stefan Wildt	GFI-102	3290
210 7590 02/27/2007 MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			EXAMINER HAMA, JOANNE	
			ART UNIT	PAPER NUMBER
			1632	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
31 DAYS		02/27/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

10/500,240

Applicant(s)

WILDT ET AL.

Examiner

Joanne Hama, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 29 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-12 and 14-65 is/are pending in the application.
- 4a) Of the above claim(s) 18-45,47-60,64 and 65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-4,6-12,14-17,46 and 61-63 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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Applicant filed a response to the Restriction Requirement of June 29, 2006 on November 29, 2006. An amended set of claims was also filed on November 29, 2006.

Claims 5, 13 are cancelled. Claims 1-3, 6, 7, 12, 33, 37, 38, 40, 43 are amended. Claims 61-65 are new. Claims 1-4, 6-12, 14-65 are pending.

Claims 47-58, 60 are withdrawn by Applicant.

Applicant's election with traverse of Group 1 in the reply filed on November 29, 2006 is acknowledged. The traversal is on the ground(s) that there is a technical relationship among the inventions that involves at least one common or corresponding technical feature (Applicant's response, page 13). With respect to method claims that have been listed in Groups I-X and XXIII and product-by-process claims listed in Groups I and XI, there is a single common inventive concept under PCT Rule 13.1: each of those methods require the technical step of "diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure"- a feature that is recited in claim 1 and required in each claim that depends from claim 1 (e.g. claims 2-44). Claim 59 (Group XXI) recites an embodiment of this common technical feature (Applicant's response, page 13). In response, this is not persuasive because while there may be a common thread amongst the inventions of "diminishing or depleting activity" of an enzyme, the restriction has been made to separate further embodiments of the claims that result in different products. Note that on page 5 of the Restriction, that while certain combinations of product and methods are analyzed together in 371 practice, the allowed combinations do not include multiple products, multiple methods of using said products and methods

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of making multiple products as claimed in the instant application (see MPEP§1850). As such, the groups remain restricted.

Applicant indicates that Nakayama et al., 1992, is irrelevant to the claimed invention because the alpha-1,6 mannosyltransferase enzyme encoded by the OCH1 gene does NOT transfer a sugar residue to a lipid-linked oligosaccharide structure, the common technical feature of the above discussed method claims (Applicant's emphasis, Applicant's response, page 13). In response, Nakayama et al. is germane to the applied claims because Nakayama et al. teach a non-human eukaryotic host comprising a mutant och1 gene. These yeast exhibit diminished or depleted activity of an enzyme that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure. The teaching of Nakayama et al. indicates that yeast having this characteristic was known at the time of filing.

As such, the claims remain restricted and claims 18-45, 59, 64, 65 are withdrawn as being drawn to non-elected subject matter.

With regard to the election of species, Applicant indicates that the following species elections were made with traverse-in-part (Applicant's response, page 15-16). Applicant indicates that traverse arises from the Examiner's characterization of certain claims being generic with respect to certain claim features (Applicant's response, page 16). For example, the Examiner states that claim 6 is generic for N-glycans, but claim 6 specifies that the host cell produces a GlcNAc3Man3GlcNAc2 structure. In response, Applicant correctly indicates that claim 6 is not generic for N-glycans because GlcNAc3Man3GlcNAc2 is a species of the genus of N-glycans. With regard to

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Applicant indicating that claim 9 is generic for diminished or depleted enzymes, claim 9 indicates that the host cell is diminished or depleted in dolichyl-P-Man:Man5GlcNAc2-PP-dolichyl alpha-1,3 mannosyltransferase activity. In response, Applicant correctly indicates that claim 9 is a species of diminished or depleted enzymes.

Applicant further notes that claim 3-27, 30 read on the elected species of CMP-Sia biosynthetic enzyme, but only claims 7-8, 17 refer to species of enzymes involved in the CMP biosynthetic pathway; claim 11, 25-27, 31 read on the elected species of the therapeutic protein, but only claim 11 and 25 refer to species of therapeutic proteins; claims 1-31 read on the elected species of the host cell, but only claims 9 and 18 refer to species of host cells (Applicant's response, page 16). In response, it is not entirely clear how Applicant's statements relate to traversal of the election of species.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18-45, 47-60, 64, 65 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 29, 2006.

Claims 1-4, 6-12, 14-17, 46, 61-63 are under consideration.

Applicant's response was not entirely responsive with regard to the species election of distinctly named N-glycans. Applicant indicated that there was only one glycan structure recited in claim 5, GlcNAc2Man3GlcNAc2 (Applicant's response, page 15). However, claim 5 has been cancelled in the amended claim set and it appears that

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claim 5 has been incorporated into claim 1. Claim 1 indicates that the claimed method results in the production of GlcNAcManXGlcNAc2 core structures, wherein X is 3, 4, or 5. It is unclear whether the elected species to be examined is GlcNAc2Man3GlcNAc2, per Applicant's response, or if another value of X was intended. Applicant is required to elect a species of GlcNAcManXGlcNAc2, wherein X is 3, 4, or 5.

In addition to this issue, Applicant's claim amendments include newly added claims, which are drawn to a new invention. As such, a subsequent restriction is required as follows. Please note that the original restriction requirement still stands and has been made FINAL above. The new restriction is necessitated by applicant's claim amendments and is supplemental to the original restriction requirement.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1a, claim(s) 1-4, 6-12, 14-17, 46, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell that expresses a glycosidase activity, the method comprising the step of diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure; wherein said method results in the production within the host cell of recombinant glycoproteins having N-glycans attached thereto comprising GlcNAcManXGlcNAc2 core structures, wherein X is 3, 4, or 5, and to a human-like glycoprotein made by said method.

Group 1b, claim(s) 1, 61-63, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell that expresses a glycosidase activity, the method comprising the step of diminishing or depleting the activity of one or more enzymes in

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the host cell that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure; wherein said method results in the production within the host cell of recombinant glycoproteins having N-glycans attached thereto comprising GICNAcManXGlcNAc<sub>2</sub> core structures, wherein X is 3, 4, or 5, wherein the host cell further comprises a GnTIII activity.

The inventions listed as Groups 1a and 1b do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: unity of invention between different categories of inventions will only be found to exist if the specific combinations are present. These combinations include:

- 1) a product and special process of manufacture of said product,
- 2) a product and a process of use of said product,
- 3) a product, a special process of manufacture of said product, and a process of use of said product,
- 4) a process and an apparatus specially designed to carry out said process,
- 5) a product, a special process of manufacture of said product, and an apparatus specially designed to carry out said process.

The allowed combinations do not include multiple products, multiple methods of using said product, and methods of making multiple products as claimed in the instant application, see MPEP § 1850. As indicated in the Restriction of June 29, 2006, Nakayama et al. 1992, The EMBO Journal, 11: 2511-2519 teach an OCH1 mutant in *S. cerevisiae*. The OCH1 mutant is an alpha-1,6 mannosyltransferase mutant (Nakayama et al., page 2516, 2<sup>nd</sup> col., 2<sup>nd</sup> parag.), which subsequently has the ability of making

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glycosylated proteins less like the yeast system and more like the mammalian system (see Cereghino and Cregg, 2000, FEMS Microbiology Reviews, 24: 45-66, see IDS; page 53, 2<sup>nd</sup> col. under "3.3 N-Linked Glycosylation").

Groups 1a and 1b are related to each others as each Group is a method of making a mammalian protein with the appropriate sugar modifications found on the mammalian protein. However, the methods are distinct from each other as each requires different and distinct steps and each result in different products. For example, Group 1b require that GnTII be used to arrive at products that are different from that of Group 1a.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions



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unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

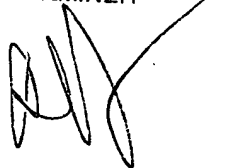
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JH

ANNE M. WEHBE' PH.D  
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'A. Wehbe', is written over the printed name and title.